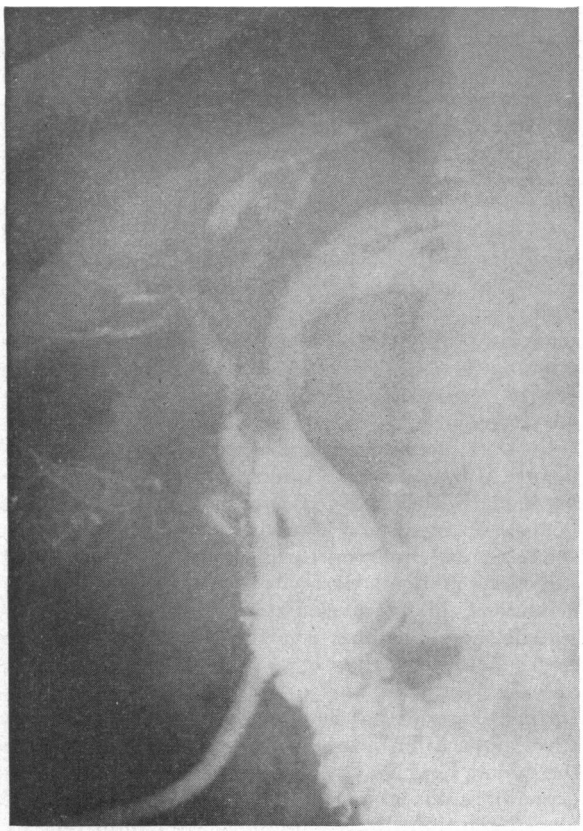

Figure 2.—Cholangiogram, four months after operation, showing return toward normal.

some compression of the lesser curvature of the stomach, evidently from the liver. The temperature ranged between 101°F. and 102°F. for three days and then became normal. The patient was treated with penicillin and was discharged after 12 days with a diagnosis of possible infectious hepatitis. Ten days later he returned because of fever and pain. This time the cephalin flocculation was 2 plus, thymol turbidity 18 units, and bilirubin 3 mg. per 100 cc. Biopsy of a specimen of the liver was reported as showing infectious hepatitis.

Pronounced jaundice continued and the patient had pain and recurrent fever. The temperature rose to 104°F. and the leukocyte content of the blood to 15,400 per cu. mm.

At operation the right lobe of the liver was observed to be practically replaced by a giant cyst. This cyst posteriorly had expanded anterior to the right kidney as a large, thin-walled mass. The common duct was approximately 4 cm. in diameter. It was opened and multiple daughter cysts of various sizes were evacuated from it. Then digital and instrumental exploration of the communicating cystic cavities in the liver was carried out. The main cyst was in the right lobe, but there were several smaller cysts in the left lobe. More than a liter of fluid and daughter cysts of varying sizes were removed and a large T-tube was left in the common duct at the conclusion of the procedure.

Pathologist's Report: The specimen was a large quantity of clear hydatid cysts, varying in diameter from 0.3 to 3 cm. Each hydatid presented a thin wall and was filled with clear, colorless fluid. Accompanying the specimens were irregular fragments of soft grayish yellow membrane, representing wall of the major hydatid cyst from the liver.

Microscopically the wall of each hydatid was observed to be composed of a thin hyaline membrane with serrated lining. In some of the sections through the hydatid, a few cross-sections of tapeworm larvae could be seen.

Diagnosis: Hydatid disease of the liver (Echinococcus granulosus).

Following operation, the septic condition very quickly subsided. As it was felt that daughter cysts were undoubtedly still present within the liver, the T-tube was irrigated daily and small cysts and cyst membranes continued to be passed. The cyst cavities shrank promptly (Figure 1). The T-tube was removed six months after operation* when cholangiograms showed an essentially normal biliary tree (Figure 2).

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Infectious Mononucleosis Complicated by Landry's Paralysis, Requiring Respirator Care

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THE SYNDROME of infectious mononucleosis was first described by Pfeiffer in 1889. He reported it as a disease of the lymph nodes of children and noted that constitutional signs and symptoms were mild. It was not until 1931 that the first reports of neurologic complications of infectious mononucleosis were made. Johansen[12] reported a case of serous meningitis with no glandular involvement and almost no abnormality in the spinal fluid. Epstein and Dameshek[3] noted a patient with stupor initially, then increased protein and cells in the cerebrospinal fluid and, two days later, splenomegaly and generalized lymphadenopathy. Atypical lymphocytes were observed in the blood. The patient was perfectly well six weeks after the onset of the illness.

Since these reports, there has been an increasing number of reports describing neurologic complications of infectious mononucleosis or glandular fever.

*When last observed, 13 months after operation, the patient was entirely asymptomatic. Upon physical examination no abnormalities suggesting recurrent or persistent trouble in the biliary tract were noted.

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Submitted August 10, 1956.

Bernstein and Wolff[1] tabulated 34 such reports in the literature from 1931 to 1947 as follows:

	Cases
Serous meningitis	4
Meningitis	10
Encephalitis	4
Meningoencephalitis	4
Meningoencephalitis and polyneuritis	7
Peripheral neuropathy	6
Optic neuritis (with papilledema without increased cerebrospinal fluid pressure)	1

Many investigators have emphasized that some of the "idiopathic" acute nervous system disorders may be associated with infectious mononucleosis, as are many cases of "aseptic meningitis." Furthermore, there may be leukopenia early, then a normal content of cells in the blood or leukocytosis with or without a relative lymphocytosis, but with atypical lymphocytes seen at some time during the course of the illness. Paul and Bunnell's description of the heterophil agglutination test in 1932 has helped immeasurably in the clarification of many of these obscure neurologic syndromes.

The majority of neurologic complications of infectious mononucleosis occur in adults. It has been observed that, even in epidemics of infectious mononucleosis, such complications develop in less than 1 per cent of patients; and in males more than in females. There may be changes in the cerebrospinal fluid without any neurologic signs whatsoever. On the other hand, acute neurologic effect may occur without demonstrable change in the cerebrospinal fluid. Bernstein and Wolff[1] stressed that complete recovery from neurologic complications in infectious mononucleosis occurs within a few days to several months in 85 per cent of all cases. However, the spinal fluid may remain abnormal for a longer period of time.

Attesting that infectious mononucleosis is not an innocuous disease and that neurologic forms may leave residual impairment, Motto[17] described a case in which a patient, with encephalitis due to infectious mononucleosis, had nystagmus and right facial paralysis 12 months after the acute phase of the disease. Bernstein and Wolff noted mild motor aphasia and difficulty in concentrating as permanent residual damage. Lawrence[14] reported that respiratory paralysis was the cause of death in seven of 16 fatal cases of infectious mononucleosis.

These reports stress the necessity for hospitalizing such patients where immediate respirator care is available. The complications may progress very rapidly; in a case reported by Durfey and Allen,[2] impairment progressed from monoplegia to complete quadriplegia with bulbar paralysis in a very short time. The case reported herewith is another example of the urgency of such precautions.

Many bizarre neurologic forms of infectious mononucleosis have been reported in the literature. Green[8] described a case of acute hemiplegia and aphasia in which the spinal fluid was completely normal. No abnormal cells were observed in the blood until two weeks after onset of the illness, when atypical lymphocytes were seen. An elevated changing heterophil titer was also noted. Geliebter[7] in 1946 described, for the first time, neurologic infectious mononucleosis in a child. The patient was a ten-year-old girl with lymphadenopathy, malaise and vomiting. There were no meningeal signs, but a lumbar puncture was carried out and the spinal fluid contained 9 mononuclear cells per cu. mm. and total protein of 400 mg. per 100 cc. Diplopia and muscular weakness followed. Poliomyelitis was considered at one time, but a changing heterophil agglutinin titer clarified the diagnosis. Walsh and co-workers[22] reported encephalitis from infectious mononucleosis in an eight-year-old boy. They also report neurologic infectious mononucleosis in an 18-month-old child, the youngest patient of record to have neurologic complications. Cerebellar symptoms also occurred in both of these patients. Walsh and co-workers emphasized that neurologic signs and symptoms may occur in any sequence with relation to other clinical evidence of infectious mononucleosis, or even without any other symptoms. Many investigators have reported neurologic complications concomitant with, days to weeks before or after other clinical manifestations of infectious mononucleosis. Walsh and co-workers further stressed that leukocytosis is not uncommon early and that, in severe neurologic cases, changes in the blood tend to be late. Bercel noted electroencephalographic abnormalities in all of five cases of neurologic infectious mononucleosis observed by him.

Ream and Hessing[19] reported a case ushered in by psychotic manifestations after a week of tenderness of lymph nodes. An electroencephalogram in this case was decidedly abnormal. Cheyne-Stokes respiration and aphasia were noted later. Kalmansohn and co-workers[13] in 1953 reported the sixth known case of coma complicating infectious mononucleosis. In the case reported it was especially interesting because the patient was 49 years of age, had no symptoms of neurologic disease and had permanent residual personality changes of considerable degree. Furthermore, there was no clinical evidence of infectious mononucleosis. However, the spinal fluid protein content was elevated and an elevated changing blood heterophil titer was reported.

An especially interesting form of neurologic infectious mononucleosis is the so-called "Guillain-Barre" syndrome. Guillain, Barre and Strohl in 1916[9] described cases of acute polyradiculoneuritis with pronounced increase in cerebrospinal fluid protein content without increase in the number of cells. This change in the spinal fluid was termed "albuminocytologic dissociation." Their criteria for the diagnosis of the syndrome were: Albuminocytologic dissociation in the cerebrospinal fluid and preponderance of motor weakness over sensory. They reported the prognosis favorable, usually with complete recovery.

In 1936, Guillain[10] stressed increased spinal fluid protein content, reporting 1,000 to 2,000 mg. of total

protein per 100 cc. as the usual finding. However, in 1937, at a symposium in Brussels, he withdrew many of his previous diagnostic criteria. Now it is conceded that hyperalbuminosis of the cerebrospinal fluid may frequently be absent in the early stages, and that it is due to local factors, such as vasodilatation and partial block to drainage of the cerebrospinal fluid due to edema and swelling of inflamed nerve roots. In addition, the outcome of this syndrome is not always benign; in 26 of 126 cases of the syndrome collected from the literature by Fox and O'Conner in 1942, the patient died. In 1949, Haymaker and Kernohan[11] concluded that there was no essential difference between the radiculoneuritis of Guillain, Barre and Strohl, and that of Landry's paralysis; they suggested the name Landry-Guillain-Barre syndrome to emphasize the possibility of fatal outcome. Raftery and co-workers[8] emphasized that evidence points to a virus as the etiologic factor in this disease, with or without a preceding respiratory tract infection. In only three of the 34 cases of the Guillain-Barre syndrome he reviewed did the patient have infectious mononucleosis; seven had upper respiratory tract infections and three had the influenzal syndrome. The remainder had no preceding illness. Garvin[6] noted that the Guillain-Barre syndrome is one of the rarer manifestations of neurologic infectious mononucleosis. Kalmansohn[13] emphasized that, in albuminocytologic dissociation of the cerebrospinal fluid, infectious mononucleosis must be differentiated from infectious neuronitis, poliomyelitis, central nervous system tumors and diabetic neuropathy. The Guillain-Barre syndrome is but one of many postinfectious encephalomyelopathic conditions.

In the few cases of neurologic infectious mononucleosis in which postmortem examination has been done,[8] engorgement of veins and capillaries of the meninges, with infiltration by mononuclear cells into the anterior nerve roots at all levels was observed. Perivascular hemorrhages, mild ganglion cell disease, moderate infiltrations by inflammatory cells in meninges and neuraxes and invasion of posterior roots and spinal ganglia have also been reported.

REPORT OF A CASE

A 14-year-old Caucasian girl was admitted to the Communicable Disease Unit of the Los Angeles County General Hospital on March 24, 1956. Two weeks previously she had had an upper respiratory tract infection with fever, nausea and headache. In four days the patient became entirely asymptomatic without treatment, and according to the physician who had attended her, there had been no abnormality in the pharynx and no splenomegaly or adenopathy. Three days before admittance, the patient began to complain of double vision and right-sided weakness. At that time leukocytes numbered 15,000 per cu. mm. of blood—84 per cent lymphocytes, 34 per cent of them being atypical. No abnormality was noted in the urine. A heterophil agglutinin titer of 1:3,000 after adsorption was reported at this time. The spinal fluid pressure was within normal limits. The fluid was clear; it contained 1 mononuclear cell per cu. mm. and the protein content was 8 mg. per 100 cc.

Two days before admission, the patient complained of stiffness of the neck. She was reexamined by the physician, who noted decreased reflexes in the left side of the abdomen and of the right knee and right ankle, in addition to nuchal rigidity. The patient was then given 40 units of zinc corticotropin (ACTH) intramuscularly daily on March 22, 23 and 24. On the day of entry to the hospital, the patient was reexamined and pronounced weakness of all four extremities and slight bulbar weakness were noted. She was, however, eating and drinking without difficulty.

Upon admittance the rectal temperature was 99.6°F, the pulse rate 100 with rhythm regular, the blood pressure 120/90 mm. of mercury, and respirations regular at the rate of 16 per minute. The patient was in acute distress, with an indistinct nasal voice and difficulty in maintaining respirations, which were shallow. The skin was normal. There was decided ptosis of the left eyelid, but the pupils were normal. Cough and gag reflexes were extremely poor but there was no pooling of pharyngeal secretions. A slight inflammation of the pharynx was noted, but no exudate. The intercostal muscles were completely paralyzed and both diaphragms were weak. There were no meningeal signs or adenopathy. There was question as to whether the spleen was enlarged; it was palpated by one examiner 1 to 2 fingerbreadths below the left costal margin.

Upon neurologic examination, complete left ophthalmoplegia, right external rectus paralysis, bilateral peripheral facial paralysis, poor gag reflex, and deviation of the protruded tongue to the left were noted. Sensations of pain and touch were apparently intact, and there was no demonstrable loss of position sense. Almost complete quadriplegia was noted, more on the right, with all muscle groups involved. The abdominal muscles were very weak, as were the diaphragms. The intercostal muscles were completely paralyzed, and the neck muscles were very weak. Biceps, triceps, knee and abdominal reflexes could not be evoked on either side. The ankle jerk was absent on the right and weak on the left. There were no pathologic reflexes.

Laboratory data

Results of laboratory tests were as follows:

March 24: The hemoglobin content of the blood was 14.2 gm. per 100 cc. Leukocytes numbered 8,500 per cu. mm.—56 per cent polymorphonuclear cells and 44 per cent lymphocytes, 11 per cent of the lymphocytes atypical. The cerebrospinal fluid was clear, contained no cells, a normal amount of sugar and gave negative reaction to a Pandy test. Blood urea nitrogen was 17.0 mg. per 100 cc., carbon dioxide combining power 26.0 mEq. per liter and potassium content 4.1 mEq. per liter. Vital capacity

was 700 cc. (normal for the patient was 2,500 cc.). Tracheotomy was done an hour after admission, and considerable pooling of pharyngeal secretions was noted. The patient was then placed in a tank type respirator and she did fairly well. An electroencephalogram was reported normal.

March 26: The hemoglobin was 12.0 gm. per 100 cc. Leukocytes numbered 9,000 per cu. mm.—37 per cent lymphocytes (11 per cent atypical), 2 per cent monocytes, and 61 per cent polymorphonuclear cells. The heterophil agglutinin titers were 1:7,168 before absorption and 1:3,584 after absorption with guinea pig kidney. (Ten days later, corresponding titers were: 1:7,168 before absorption and 1:1,792 after guinea pig kidney absorption.) The cerebrospinal fluid heterophil titer was reported as negative. The fluid contained 1 mononuclear cell per cu. mm., a normal amount of sugar and total protein of 40 mg. per 100 cc. There was 1 plus reaction to a Pandy test. Protein-bound iodine was 7.5 micrograms per 100 cc. of blood, cholesterol 145 mg. per 100 cc. and the I^{131} uptake was 9.6 per cent. X-ray films of the chest (taken March 26 and 28) were normal. Urine cultures grew gamma streptococcus and Staphylococcus albus.

April 4: Bromsulfalein retention after 45 minutes was nil. Thymol turbidity was 4 units; alkaline phosphatase, 3.5 Bodansky units; clotting time normal.

The patient improved rapidly. On March 29 the speech was noted to be improved. On April 1 the facial paralysis was less noticeable, and the patient was able to move both upper extremities for the first time. By April 17 she could be out of the respirator for eight hours daily and nine days later she had no further need of it.

On April 15 the protein-bound iodine content of the blood was 11.6 micrograms per 100 cc. A culture of the urine on that date again grew gamma streptococcus and Staphylococcus albus.

The patient was discharged on May 23, two months after admission. There was then no significant muscular weakness or other residual impairment, and she was walking fairly well. An encephalogram showed no abnormality. The final diagnosis was infectious mononucleosis with encephalomyelitis (and Landry's paralysis). The patient was given 20 cc. of gamma globulin intramuscularly on the day of admission, and 2,000 micrograms of vitamin B_{12} daily intramuscularly. Otherwise, treatment was entirely symptomatic.

DISCUSSION

The Paul-Bunnell, or heterophil agglutinin test is of especial importance in the diagnosis of infectious mononucleosis, but in a large proportion of cases elevation of titer does not occur. Raftery and co-workers[18] observed that the highest incidence of elevated heterophil agglutinin titer occurred in the second week of the disease, but even at that period there was no significant elevation in 40 per cent of proved cases. After the third week of the illness, elevation of titer occurred in less than 50 per cent of proved cases. Observation of atypical lymphocytes in a specimen of blood often is the only clue to the diagnosis, as in the case presented by Librach.[15] Since a heterophil agglutinin titer of 1:7 to 1:56 before absorption occurs in 80 to 90 per cent of normal persons, differential absorption is often of great help in differentiating infectious mononucleosis from normal states and from serum sickness (in which the titer may be quite high). The differential is as follows:

Normal serum—Absorbed by guinea pig kidney.
Serum from person with serum sickness—Absorbed by guinea pig kidney and beef red blood cells.
Serum from person with infectious mononucleosis—Absorbed by beef red blood cells, but *not* absorbed by guinea pig kidney.

However, according to Raftery[18] the titer of agglutination may vary because of variations in the sheep red blood cell suspensions used, not all sheep having blood of the same value. Moreover, in many cases serum from normal persons contains cold agglutinins for sheep red blood cells. Therefore, the test tubes used in performing the test should be warmed gently. Serial titration tests are especially useful in the diagnosis of infectious mononucleosis.

In 1948, Silberstein and co-workers[20] described the phenomenon of the presence of heterophil antibodies in the cerebrospinal fluid of patients with neurologic forms of infectious mononucleosis. Many investigators since then have not been able to verify the findings, although a few have. Silberstein described a positive qualitative heterophil reaction, but it remained for Freedman and co-workers[5] to describe a positive quantitative heterophil agglutinin titer of 1:28 in the spinal fluid of a patient observed by them. They emphasized how insensitive this test is when done on the spinal fluid, the blood heterophil titer concurrently being much higher.

The differential diagnosis of lymphocytic meningitis and neurologic infectious mononucleosis without lymph node involvement is often puzzling, but can be resolved, as was emphasized by Tidy,[21] by serial heterophil titration tests and observation of "Downey" cells in specimens of blood. Librach[16] urged that in all cases presumptive of poliomyelitis, serial heterophil tests and cytologic examination of the blood be carried out with infectious mononucleosis in mind. Moreover, the disease cannot be considered limited to persons of a particular age group: Fiese and co-workers[22] reported a case of neurologic infectious mononucleosis in a 58-year-old man, and Walsh[22] a case in an 18-month-old child.

The case presented in this report is especially interesting from several aspects:

1. The almost complete lack of clinical symptoms pointing to infectious mononucleosis. (The diagnosis might have been missed had the physician not ordered the necessary blood studies.)

2. The completely normal cerebrospinal fluid in the face of such extensive neurologic involvement.

3. Speculation as to the role corticotropin might have had in the course of the disease.

4. The sudden and extremely rapid severe involvement of practically every voluntary muscle group in the body, without apparent sensory involvement.

5. The extremely high heterophil agglutinin titer in the serum concomitant with "negative" titer in the cerebrospinal fluid.

6. The necessity for the use of a respirator for one month during the course of the illness.

7. The complete recovery of the patient in a period of two months, without residual effect.

Fiese and co-workers[4] used cortisone in treatment and speculated on the effect the drug may have had on the rapid recovery of the patient. However, they acknowledged the possibility that spontaneous recovery would have occurred as rapidly.

CONCLUSIONS

With the exception of bacterial meningitis, infectious mononucleosis must be considered in every acute neurologic syndrome whether or not there are changes in the cerebrospinal fluid—in patients of any age. Clinical manifestations such as enlarged lymph nodes, exudative pharyngitis or splenomegaly may be entirely absent throughout the course of the disease. The only clue to the diagnosis may be an elevated heterophil titer, or the presence of atypical lymphocytes or "Downey" cells in the blood. Leukocytes may be increased in number and the cell differential abnormal, but not necessarily.

Emphasis should be put upon the fact that the condition of patients with neurologic infectious mononucleosis may progress extremely rapidly—in a period of hours or days. These patients should be observed constantly in a hospital where tracheotomy and respirator care are instantly available.

The use of cortisone or corticotropin (ACTH) for treatment of patients with undiagnosed acute neuropathic conditions may be dangerous.

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Contact Ulcer of the Larynx

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THERE IS MUCH CONFUSION among laryngologists as to the etiology of contact ulcer of the larynx. Jackson[1] noted that the disease is often mistaken for some other condition. Contact ulcer has been attributed to constant or severe over-use of the voice and to environmental, occupational or habitual exposure to dust, grit, smoke or chemical irritants.

While it is true that the larynx reacts very sensitively to adverse conditions that put a strain on it either through local irritants or by undermining the general physical condition, contact ulcer in the strict sense of the word does not usually occur unless an element of emotional stress is present. Emotional upheavals may influence the biochemical changes taking place in the larynx, thus making the vocal cords a prey to pathological changes. Moses,[2] in an article titled "Vocal Cord Neurosis," said that contact ulcer had too long been considered the result of abuse of the voice, and he expressed belief that allergic sensitivity plays an important role. He cited the case of a singer with a normal larynx who developed a large